UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualification:-

M.Sc.

Bioprocessing G1: Downstream Processing

COURSE CODE	:	**BENGEG01**
DATE	:	**16-MAY-06**
TIME	:	**10.00**
TIME ALLOWED	:	**3 Hours**

06-C0122-3-30

TURN OVER

Answer ***FOUR QUESTIONS. ALL*** *questions carry a total of* ***25 MARKS*** *each, distributed as shown* [ ]. *Only the* ***FIRST FOUR ANSWERS*** *will be marked.*

1.

a) Rotary Vacuum Filtration is used in the large-scale removal of solids from fermentation broths. Provide an engineering analysis of this technology which details the most important operating characteristics as well as those areas of potential product loss. [10]

b) Selection of body feed and pre-coat materials are crucial in determining filtration performance. With the aid of suitable stretches describe the most important effects. [5]

c) The filtration behaviour of biological suspensions differs from that predicted by theory. Why is this so? Provide three reasons why this can be the case together with appropriate engineering relationships that capture these effects. [10]

2.

a) How does expanded bed adsorption differ from classical packed bed approaches? [10]

b) How is bed voidage related to the height of expansion in an expanded bed system. [5]

c) Why is Stokes Law of settling important when defining the behaviour of an expanded bed? [5]

d) Discuss briefly the impact of operating an expanded bed in downflow during elution on likely performance relative to operation under expanded conditions at all times. [5]

3.

a) What is meant by the cut-off characteristics of a filtration membrane? How does this relate to a membrane's ability to achieve fractionation? [5]

b) Centrifuge designs aim to increase the speed of particle separation by two different approaches. What are these? Using examples of industrially relevant machines, illustrate briefly how these approaches are realised in the design of machines. [10]

c) During the centrifugal recovery of a broth containing cells which express an inclusion body, a loss of product has been noted. Why might this be the case? Can you suggest any changes that might be made to the fermentation to reduce this loss? [10]

PLEASE TURN OVER

4.

A 10000 L vessel (height equals diameter) equipped with baffles and a turbine impeller (diameter one-third of vessel diameter, stirrer speed 10 rpm) is to be used in a process for the fractionation of human blood plasma by selective precipitation of proteins. The precipitation is achieved by adjustment of pH and then use of ethanol to a final concentration of 20% v/v. The precipitate suspension is to be held overnight (~ 12 hours) before separation by centrifugation within a 6 hour shift. The suspension is to be fed by overhead air pressure to a disc stack centrifuge. Both the soluble and precipitated proteins are to be used as the basis of human therapies after further purification steps using chromatography columns.

a) Prepare a detailed appraisal of the design of the precipitation vessel and list any concerns on its suitability for this process. [10]

b) Design a small reactor operating at the 100 mL scale to yield a similar feed stream for the centrifugation stage as will be prepared at full scale. [10]

c) Prepare a flowsheet in the form of equipment layout for the whole precipitation and centrifugal separation process. Discuss how this whole process might be mimicked at the bench scale with the 100 mL reactor defining scale of operation. [5]

Give full details of all assumptions made in your design calculations.

Density of precipitate suspension 900 kg m^{-3}
Viscosity of precipitate suspension 0.004 N s m^{-2}

5.

a) The recovery of a pharmaceutical intermediate, NA491, direct from an enzymatic bioconversion medium is to be attempted by liquid-liquid extraction. If this is to be performed counter-currently derive a suitable operating line equation for the process. Clearly state any assumptions made. [10]

b) At the end of the bioconversion NA491 is synthesised to a concentration of 65 g kg^{-1}. Hexadecane has been identified as the most suitable solvent for extraction giving an equilibrium distribution coefficient of 5. If a 99% w/w recovery and a four-fold increase in the concentration of NA491 in the solvent extract are necessary calculate the number of theoretical stages required. Clearly state any assumptions made. [8]

c) Describe the operation of an appropriate phase contactor for this process and justify your choice of equipment. [7]

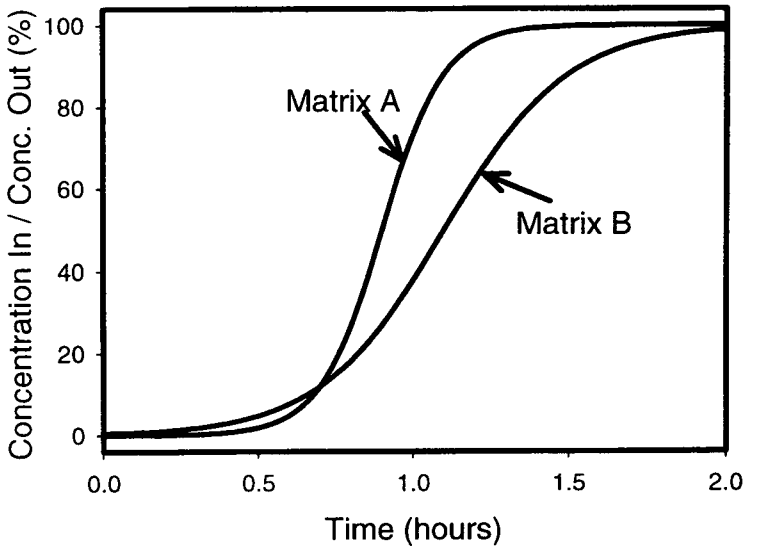
A sheet of graph paper is supplied.

CONTINUED

6.

Trials to examine the best protein A chromatography matrix for purifying an antibody are being carried out. To look at capacity for antibody, experiments with pure antibody have been carried out. One set of results is given below at the following conditions:
Flow rate – 10ml/min
Antibody Concentration – 0.5mg/ml
Column Volume – 10ml

Concentration of Antibody at Column Exit vs. Time



a) Which of the 2 matrices has the higher dynamic capacity at 2% breakthrough and what is this capacity (in g product / L matrix)? [8]

b) Which has the higher equilibrium / static capacity? What factors could lead to differences between static and dynamic capacity, which is the most likely in this case? [8]

c) Sketch the graph shown adding two more breakthrough profiles when the same is carried out at double the flowrate. Briefly describe your reasoning. [7]

d) Give 2 other parameters that should measured as well as capacity to determine the better matrix. [2]

END OF PAPER